Diastereodivergent Combined Carbometalation/Zinc Homologation/C-C Fragmentation Reaction as an Efficient Tool to Prepare Acyclic Allylic Quaternary Carbon Stereocenters

Sudipta Raha Roy, Dorian Didier, Amir Kleiner and Ilan Marek*

The Mallat Family Laboratory of Organic Chemistry, Schulich Faculty of Chemistry and Lise Meitner-Minerva Center for Computational Quantum Chemistry, Technion-Israel Institute of Technology, Technion City, Haifa 32000, Israel.

Table of Contents:

General Considerations: 1
Experimental Section:
  Synthesis of benzyl 2-diazoacetate: 1
  General procedure for the preparation of cyclopropene carboxylates: 1
  Synthesis of benzyl 2-(4-methylpent-3-en-1-yl)cycloprop-2-ene-1-carboxylate (Ii): 1
  Synthesis of enantioenriched cyclopropene: 2
  Optimization of reaction conditions: 3
  Procedure for the synthesis of 2a_anti: 4
  Procedure for the synthesis of 2a_syn: 4
  General procedure for anti-Carbometalation/Zinc-Homologation/Ring opening of cyclopropanes: 4
  General procedure for syn-Carbometalation/Zinc-Homologation/Ring opening of cyclopropanes: 4
  General procedure for the ozonolysis of 4b, 4g, 4h and 4i: 5
Characterization of starting materials: 5-7
Characterization of compounds: 8-12
NMR spectra and HPLC analysis: 13-54
General Considerations:
All glassware was flame dried under vacuum, and cooled under argon prior to use. Unless otherwise stated, all reactions were carried out under positive pressure of argon. Ether and THF were dried from Pure-Solv® Purification System (Innovative Technology©). Dichloromethane was distilled from CaH₂. Toluene was distilled from sodium and benzophenone. Copper iodide, rhodium acetate dimer, methyllithium (1.6 M in diethyl ether), butyllithium (1.6 M in hexane), hexyllithium (2.3 M in hexane), phenyllithium (1.9 M in dibutyl ether), methylmagnesium bromide (3.0 M in diethyl ether), vinylmagnesium bromide (1.0 M in THF) and diethylzinc (1 M in hexane) were purchased from Aldrich. Thin Layer Chromatography (TLC) was performed using Merck© silica gel 60 F254 plates and visualized by exposure to UV light (254 nm) or stained with anisaldehyde, phosphomolybdic acid, or potassium permanganate. Column chromatography was performed using Bio-Lab silica gel 60A (0.040-0.063 mm). ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker© spectrometers AVIII400, using CDCl₃ as a solvent. NMR data were processed with Topspin or with NMRnotebook. Peak multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m= multiplet. GC-MS was performed on Thermo Scientific™ Ion Trap GC/MS: ITQTM 900 with a Varian Factor Four Capillary column (VF-5 ms, 30 m x 0.25 mm). HPLC chromatograms were recorded using Agilent© 1100 Series line with CHIRALPAK® AD-H, AY-H, IA or CHIRALCEL® OD columns. Optical rotation were measured using SCHMIDT and HAENSCH© Unipol L1000 with [α]D values reported in degrees; concentration (c) is in g/100 mL.

Experimental section:

Synthesis of benzyl 2-diazoacetate:
The benzyl 2-diazoacetate was synthesized from benzyl acetoacetate by following the reported procedure.¹

General procedure for the preparation of cyclopropene carboxylates:
Following the reported procedure² cyclopropene carboxylates were prepared from the reaction of alkyne³ and alkyl 2-diazoacetate.

Synthesis of benzyl 2-(4-methylpent-3-en-1-yl)cycloprop-2-ene-1-carboxylate (1i):
Title compound was synthesized following the reported procedures as mentioned in the following scheme.

---

³ All alkynes were commercially available except tert-butylidimethyl(pent-4-yn-1-yloxy)silane which was prepared according to the reported procedure (L. Cleary, H. Yoo and K. J. She, Org. Lett., 2011, 7, 1781).
Then Swern oxidation was performed with 1ga. Oxalyl chloride (1.25 eq, 0.54 mL, 6.25 mmol) was dissolved in 20 mL of DCM and kept at -78 °C. Then DMSO (2.5 eq, 0.89 mL, 12.5 mmol; solution was prepared in 5 mL DCM) was added dropwise and stirred for 30 min. Then 1ga (1 eq, 1.16 g, 5 mmol; solution was prepared in 5 mL DCM) was added and stirred for 1 h. Then triethylamine (6 eq, 4.1 mL, 30 mmol) was added and stirred overnight. The mixture was then diluted with 20 mL DCM and poured over 10 mL of a saturated aqueous solution of NH₄Cl. The organic layer was separated and dried over Na₂SO₄ and concentrated in vacuum to yield a crude oil which was further purified by flash column chromatography (hexane/ EtOAc, 99:1) to get 1gb in 95% yield (1.1 g).

Finally the Wittig reaction was performed with 1gb to get the title compound. Isopropyl triphenylphosphonium bromide salt was prepared separately from the reaction of triphenylphosphine and 2-bromopropane. To a cooled mixture (0 °C) of isopropyltriphenylphosphonium bromide (1.2 eq, 927 mg, 2.4 mmol) in 10 mL of dry Et₂O (ca. 10 mL) was added nBuLi (1.2 eq, 2.4 mmol, 1.6 M in hexane) under inert atmosphere. The solution turned red due to the formation of the corresponding ylide. After the mixture was stirred for 1 h at room temperature, a solution of the aldehyde 1gb (1 eq, 461 mg, 2 mmol) in 5 mL of dry Et₂O was added dropwise and stirring was continued at room temperature. The reaction mixture was monitored by TLC. After completion of the reaction hexane was added to the reaction mixture to precipitate the triphenylphosphine oxide (Ph₃PO). After filtration, the solution was concentrated, and the residue was purified by flash column chromatography (hexane/ EtOAc, 99:1) to get the compound 1i in 62% yield (320 mg).

**Synthesis of enantioenriched cyclopropene:**

Rh₂(OAc)(R,R-DPTI)₃ (DPTI = diphenyltriflylimidazolidinone) which was prepared following the reported procedure, was used as a chiral catalyst for the synthesis of enantioenriched cyclopropene. To a flame dried 3-necked 100ml round bottom flask equipped with a Teflon stirring bar under argon atmosphere Rh₂(OAc)(R,R-DPTI)₃ (0.5 mol%, 6.86 mg) was added and dissolved in 9 mL of dry DCM, followed by the addition of alkyn (10 eq, 10 mmol). Then a solution of methyl 2-diazo-2-phenylacetate (1 mmol in 7 mL DCM) was added to the reaction mixture through a syringe pump with 0.5 mL/h flow rate. The reaction was followed by TLC until disappearance of alkyl 2-diazoacetate (eluent hexane/EtOAc, 9:1). The solvent was evaporated and the resulting mixture purified by column chromatography (hexane/ EtOAc, 95:5) to afford the enantioenriched cyclopropene product as clear color less oil. Following this procedure all the enantioenriched cyclopropene 1b, 1e and 1f were synthesized.

The absolute configuration of the 1f was determined by comparing the optical rotation described in the literature with an authentic sample after reduction into the corresponding alcohol with DIBAL. Characterization and spectral data of the alcohol was compatible with literature data. The absolute configuration of the 1b and 1e was assumed to be the same of the analogous 1f.

---


Optimization of reaction conditions:

Table S-1: Combined anti-carbometalation – zinc homologation – fragmentation reactions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>2a&lt;sub&gt;anti&lt;/sub&gt; / 4a&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>---</td>
<td>27:73</td>
</tr>
<tr>
<td>2</td>
<td>L&lt;sub&gt;1&lt;/sub&gt;</td>
<td>12:88</td>
</tr>
<tr>
<td>3</td>
<td>L&lt;sub&gt;2&lt;/sub&gt;</td>
<td>13:87</td>
</tr>
<tr>
<td>4</td>
<td>L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>06:94 (72)</td>
</tr>
</tbody>
</table>

<sup>a</sup> 1a was consumed completely and the ratio between products 2a<sub>anti</sub> and 4a was determined by GC-MS of the crude reaction mixture. Parentheses represent isolated yield after purification by column chromatography.

Table S-2: Combined syn-carbometalation – zinc homologation – fragmentation reactions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Me[M]</th>
<th>Solvent-A</th>
<th>Solvent-B</th>
<th>X:Y</th>
<th>Ligand</th>
<th>2a&lt;sub&gt;syn&lt;/sub&gt; / 4a&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeLi</td>
<td>PhMe</td>
<td>---</td>
<td>---</td>
<td>L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>67:33</td>
</tr>
<tr>
<td>2</td>
<td>MeLi</td>
<td>PhMe</td>
<td>THF</td>
<td>1:1</td>
<td>L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>61:39</td>
</tr>
<tr>
<td>3</td>
<td>MeLi</td>
<td>PhMe</td>
<td>THF</td>
<td>1:2</td>
<td>L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>45:55</td>
</tr>
<tr>
<td>4</td>
<td>MeMgBr</td>
<td>Et&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>THF</td>
<td>1:2</td>
<td>L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>73:27</td>
</tr>
<tr>
<td>5</td>
<td>MeMgBr</td>
<td>PhMe</td>
<td>THF</td>
<td>1:2</td>
<td>L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>80:20</td>
</tr>
<tr>
<td>6</td>
<td>MeLi</td>
<td>PhMe</td>
<td>THF</td>
<td>1:2</td>
<td>L&lt;sub&gt;4&lt;/sub&gt;</td>
<td>88:12</td>
</tr>
<tr>
<td>7</td>
<td>MeLi</td>
<td>PhMe</td>
<td>THF</td>
<td>1:2</td>
<td>L&lt;sub&gt;5&lt;/sub&gt;</td>
<td>60:40</td>
</tr>
<tr>
<td>8</td>
<td>MeLi</td>
<td>PhMe</td>
<td>THF</td>
<td>1:2</td>
<td>L&lt;sub&gt;6&lt;/sub&gt;</td>
<td>11:89 (65)</td>
</tr>
<tr>
<td>9</td>
<td>MeLi</td>
<td>PhMe</td>
<td>THF</td>
<td>1:2</td>
<td>--</td>
<td>80:20</td>
</tr>
</tbody>
</table>

<sup>a</sup> 1a was consumed completely and ratio between products 2a<sub>syn</sub> and 4a was determined by GC-MS of the crude reaction mixture. Parentheses represent isolated yield after purification by column chromatography.
Procedure for the synthesis of 2a_{anti}:
To a suspension of Cul (100 mg, 1.05 equiv, 0.525 mmol) in 6 mL of THF, MeLi was added drop-wise at -45 °C (1.05 equiv, 0.525 mmol). The reaction mixture was allowed to stir for 30 min after which the 1a (1 equiv, 115 mg, 0.5 mmol, dissolved in 2 ml of THF) was added drop-wise at that temperature and the reaction mixture was stirred until TLC shows complete consumption of the starting cyclopropene (eluant Hexane:Et₂O = 95:5 ca. 30 min). The reaction was then quenched with an aqueous solution of NH₄Cl/NH₂OH (2:1). The aqueous layer was extracted twice with Et₂O and the combined organic phases were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Crude mixtures were then purified by flash chromatography using hexane/ Et₂O as eluent to get the compound 2a_{anti} in 75% yield (93 mg).

Procedure for the synthesis of 2a_{syn}:
To a suspension of Cul (100 mg, 1.05 equiv, 0.525 mmol) in 6 mL of PhMe, MeLi was added drop-wise at -45 °C (1.05 equiv, 0.525 mmol). The reaction mixture was allowed to stir for 30 min after which the 1a (1 equiv, 115 mg, 0.5 mmol, dissolved in 2 ml of PhMe) was added drop-wise at that temperature and the reaction mixture was stirred until TLC shows complete consumption of the starting cyclopropene (eluant Hexane:Et₂O = 95:5 ca. 30 min). The reaction was then quenched with an aqueous solution of NH₄Cl/NH₂OH (2:1). The aqueous layer was extracted twice with Et₂O and the combined organic phases were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Crude mixtures were then purified by flash chromatography using hexane/ Et₂O as eluent to get the compound 2a_{syn} in 72% yield (90 mg).

General procedure for anti-Carbometalation/Zinc-Homologation/Ring opening of cyclopropanes:
To a suspension of Cul (0.1 g, 1.05 equiv, 0.525 mmol) in 8 mL of THF, alkylolithium was added drop-wise at -45 °C (1.05 equiv, 0.525 mmol). The reaction mixture was allowed to stir for 30 min after which the cyclopropene (1 equiv, 0.5 mmol, dissolved in 2 ml of THF) was added drop-wise at that temperature and the reaction mixture was stirred until TLC shows complete consumption of the starting cyclopropene (eluant Hexane:Et₂O = 95:5 ca. 30 min). Then, to the reaction mixture CH₂I₂ (0.1 mL, 2.5 equiv, 1.25 mmol) was added followed by the drop-wise addition of Et₂Zn (2.5 equiv, 1.25 mmol) and 1,10-phenanthroline (0.095 g, 1.05 equiv, 0.525 mmol, dissolved in 3 ml of THF). The resulting reacting mixture (dark yellow to brown in case of MeLi) was stirred at this temperature and slowly warmed up to 20 °C (ca. 2h). The reaction was then quenched with an aqueous solution of NH₄Cl/NH₂OH (2:1). The aqueous layer was extracted twice with Et₂O and the combined organic phases were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Crude mixtures were then purified by flash chromatography using hexane/ Et₂O as eluent.

General procedure for syn-Carbometalation/Zinc-Homologation/Ring opening of cyclopropanes:
To a suspension of Cul (0.1 g, 1.05 equiv, 0.525 mmol) in 6 mL of PhMe, alkylolithium was added drop-wise at -45 °C (1.05 equiv, 0.525 mmol). The reaction mixture was allowed to stir for 30 min after which the cyclopropene (1 equiv, 0.5 mmol, dissolved in 2 ml of PhMe) was added drop-wise at that temperature and the reaction mixture was stirred until TLC shows complete consumption of the starting cyclopropene (eluant Hexane:Et₂O = 95:5 ca. 30 min). Then to that reaction mixture THF (16 mL) and CH₂I₂ (0.1 mL, 2.5 equiv, 1.25 mmol) was added followed by the drop-wise addition of Et₂Zn (2.5 equiv, 1.25 mmol) and 1,10-phenanthroline (0.095 g, 1.05 equiv, 0.525 mmol, dissolved in 3 ml of THF). The resulting reacting mixture (dark yellow to brown in case of MeLi) was stirred at this temperature and slowly warmed up to -20 °C (ca. 2h). The reaction was then quenched with an aqueous solution of
NH₄Cl/NH₃OH (2:1). The aqueous layer was extracted twice with Et₂O and the combined organic phases were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Crude mixtures were then purified by flash chromatography using hexane/ Et₂O as eluent.

**General procedure for the ozonolysis of 4b, 4g, 4h and 4i:**
The determination of the enantiomeric excess of 4b, 4g, 4h and 4i could not be done by HPLC with CHIRALPAK® AD-H, AY-H, IA or CHIRALCEL® OD columns. Therefore ozonolysis was performed on the 4b, 4g, 4h and 4i to convert them into the corresponding aldehyde 5b, 5g, 5h and 5i.

4 (1 eq, 0.25 mmol) was dissolved in 7 mL of DCM and kept at -78 °C. Then ozone was purged to the solution until reaction mixture turn into pale blue colour (ca. 5 min). Triphenylphosphine (4 eq, 262 mg, 1 mmol) was added at a time and kept at that temperature for 30 min then at rt for 12h. The mixture was then concentrated in vacuo and further purified by flash column chromatography (hexane/ EtOAc, 90:10) to get the desired 5.

**Characterization of starting materials:**

**Benzyl 2-butylocyclopent-2-ene-1-carboxylate (1a):**

\[
\text{R}_1 = 0.57 \text{ (Hexane/Et}_2\text{O = 94:6); Yield: 65\% (Colorless oil)}
\]

\[\text{^1H NMR (400 MHz, CDCl}_3\): } \delta = 2.04 (\text{d, } J = 1.2 \text{ Hz, 1H}), 2.63-2.76 (\text{m, 4H}), 4.93 (\text{d, } J = 12.4 \text{ Hz, 1H}), 4.98 (\text{d, } J = 12.4 \text{ Hz, 1H}), 6.20 (\text{d, } J = 12.4 \text{ Hz, 1H}), 7.02-7.06 \text{ (m, 3H), 7.09-7.12 (m, 2H), 7.14-7.20 (m, 5H); ^1^C NMR (100 MHz, CDCl}_3\): } \delta = 19.9, 26.7, 32.9, 66.1, 94.9, 114.8, 126.3, 128.0, 128.1, 128.3, 128.4, 128.5, 136.4, 140.6, 176.2; HRMS (ESI) calcd. for C_{19}H_{17}O_2 [M+H]^+: 279.1350; found: 279.1350.

**Benzyl 2-phenethylcyclopent-2-ene-1-carboxylate (1b):**

\[
\text{R}_1 = 0.43 \text{ (Hexane/Et}_2\text{O = 94:6); Yield: 62\% (Colorless oil)}
\]

\[\text{^1H NMR (400 MHz, CDCl}_3\): } \delta = 2.04 (\text{d, } J = 1.2 \text{ Hz, 1H}), 2.63-2.76 (\text{m, 4H}), 4.93 (\text{d, } J = 12.4 \text{ Hz, 1H}), 4.98 (\text{d, } J = 12.4 \text{ Hz, 1H}), 6.20 (\text{d, } J = 12.4 \text{ Hz, 1H}), 7.02-7.06 \text{ (m, 3H), 7.09-7.12 (m, 2H), 7.14-7.20 (m, 5H); ^1^C NMR (100 MHz, CDCl}_3\): } \delta = 19.9, 26.7, 32.9, 66.1, 94.9, 114.8, 126.3, 128.0, 128.1, 128.3, 128.4, 128.5, 136.4, 140.6, 176.2; HRMS (ESI) calcd. for C_{19}H_{17}O_2 [M+H]^+: 279.1350; found: 279.1350.

**Ethyl 2-phenethylcyclopent-2-ene-1-carboxylate^6 (1c):**

\[
\text{R}_1 = 0.52 \text{ (Hexane/Et}_2\text{O = 94:6); Yield: 60\% (Colorless oil)}
\]

\[\text{^1H NMR (400 MHz, CDCl}_3\): } \delta = 1.25 (\text{t, } J = 7.2 \text{ Hz, 3H}), 2.14 (\text{d, } J = 1.2 \text{ Hz, 1H}), 2.79-2.84 \text{ (m, 2H), 2.88-2.93 (m, 2H), 4.08-4.17 (m, 2H), 6.35 (d, } J = 1.2 \text{ Hz, 1H), 7.19-7.22 \text{ (m, 3H), 7.25-7.31 (m, 2H); ^1^C NMR (100 MHz, CDCl}_3\): } \delta = 14.4, 19.9, 26.8, 32.9, 60.2, 94.9, 114.9, 126.2, 128.3, 128.4, 140.7, 176.4; HRMS (ESI) calcd. for C_{19}H_{17}O_2 [M+H]^+: 217.1262; found: 217.1223.

---

Ethyl 2-benzylocycloprop-2-ene-1-carboxylate (1d):

\[
\text{CO}_2\text{Et}
\]

Rf = 0.52 (Hexane/EtO = 94:6); Yield: 61% (Colorless oil)

1H NMR (400 MHz, CDCl3): δ = 1.13 (t, J = 7.2 Hz, 3H), 2.15 (d, J = 1.6 Hz, 1H), 3.77 (q, J = 17.6 Hz, 2H), 3.98-4.04 (m, 2H), 6.39 (d, J = 1.2 Hz, 1H), 7.15-7.19 (m, 3H), 7.22-7.26 (m, 2H); 13C NMR (100 MHz, CDCl3): δ = 14.5, 20.6, 31.6, 60.4, 95.8, 114.8, 126.9, 128.8 (x2), 136.4, 176.2; HRMS (ESI) calcd. for C13H14NaO2 [M+Na]+: 225.0932; found: 225.0886.

Benzy1 2-benzylocycloprop-2-ene-1-carboxylate (1e):

\[
\text{CO}_2\text{Bn}
\]

Rf = 0.51 (Hexane/EtO = 95:5); Yield: 63% (Colorless oil)

1H NMR (400 MHz, CDCl3): 2.25 (d, J = 1.6 Hz, 1H), 3.74 (d, J = 17.6 Hz, 1H), 3.84 (d, J = 17.6 Hz, 1H), 5.04 (s, 2H), 6.43 (d, J = 1.2 Hz, 1H), 7.19-7.24 (m, 3H), 7.25-7.32 (m, 7H); 13C NMR (100 MHz, CDCl3): δ = 20.4, 31.4, 66.1, 95.6, 114.5, 126.8, 128.0, 128.0, 128.5, 128.6, 128.7, 136.1, 136.6, 175.9; HRMS (ESI) calcd. for C18H17O2 [M+H]+: 265.1287; found: 265.1223.

(S)-Benzy1 2-benzylocycloprop-2-ene-1-carboxylate (1f):

\[
\text{CO}_2\text{Bn}
\]

Rf = 0.51 (Hexane/EtO = 95:5); Yield: 80% (Colorless oil)

Spectral data of the title compound were identical to the racemic sample. e.r. = 93:7.

The chiral sample was analyzed by HPLC using a CHIRALCEL® OD column (4.6mmØx250mmL), n-hexane/isopropanol 99:1, 1 mL/min, 210nm. tR (major) = 16.53 min, tR (minor) = 14.98 min. [α]D2: (CHCl3, c = 0.30): 3.64°.

Benzy1 2-hexycycloprop-2-ene-1-carboxylate (1f):

\[
\text{Hex}
\]

Rf = 0.62 (Hexane/EtO = 94:6); Yield: 64% (Colorless oil)

1H NMR (400 MHz, CDCl3): 0.88 (t, J = 7.2 Hz, 3H), 1.24-1.36 (m, 6H), 1.52-1.58 (m, 2H), 2.19 (d, J = 1.2 Hz, 1H), 2.46-2.50 (m, 2H), 5.09 (d, J = 12.8 Hz, 1H), 5.14 (d, J = 12.8 Hz, 1H), 6.33 (d, J = 1.2 Hz, 1H), 7.31-7.36 (m, 5H); 13C NMR (100 MHz, CDCl3): δ = 14.0, 19.7, 22.5, 24.9, 26.6, 28.8, 31.5, 66.0, 93.8, 115.6, 128.0, 128.1, 128.5, 136.5, 176.5; HRMS (ESI) calcd. for C19H22NaO2 [M+Na]+: 281.1563; found: 281.1512.

(S)-Benzy1 2-hexycycloprop-2-ene-1-carboxylate (1f):

\[
\text{Hex}
\]

Rf = 0.62 (Hexane/EtO = 94:6); Yield: 82% (Pale pellony oil)

Spectral data of the title compound were identical to the racemic sample. e.r. = 91:9.

The chiral sample was analyzed by HPLC using a CHIRALPAK® IA column (4.6mmØx250mmL), n-hexane/isopropanol 99:1, 1 mL/min, 210 nm. tR (major) = 6.30 min, tR (minor) = 6.76 min. [α]D2: (CHCl3, c = 0.42): 12.08°.

Benzy1 2-(3-((tetr-butyldimethylsilyl)oxy)propyl)cycloprop-2-ene-1-carboxylate (1g):

\[
\text{OTBDMS}
\]

Rf = 0.67 (Hexane/EtO = 95:5); Yield: 65% (Colorless oil)

1H NMR (400 MHz, CDCl3): 0.03 (s, 6H), 0.88 (s, 9H), 1.74-1.81 (m, 2H), 2.19 (d, J = 1.2 Hz, 1H), 2.57 (t, J = 7.2 Hz, 2H), 3.61-3.65 (m, 2H), 5.09 (d, J = 12.4 Hz, 1H), 5.14 (d, J = 12.4 Hz, 1H), 6.35 (d, J = 1.2 Hz, 1H), 7.28-7.37 (m, 5H); 13C NMR (100 MHz, CDCl3): δ = -5.3 (x2), 18.3, 19.8, 21.5, 25.9 (x3), 29.8, 31.9, 61.9, 66.0, 94.2, 115.2, 128.0, 128.1, 128.5, 136.4, 176.4; HRMS (ESI) calcd. for C29H31O5Si [M+H]+: 347.1968; found: 347.2037.

---

Benzyl 2-(3-chloropropyl)cycloprop-2-ene-1-carboxylate (1h):

R_f = 0.47 (Hexane/Et_2O = 95:5); Yield: 63% (Colorless oil)

^1H NMR (400 MHz, CDCl_3): 2.00-2.06 (m, 2H), 2.22 (d, J = 1.6 Hz, 1H), 2.66-2.71 (m, 2H), 3.53-3.60 (m, 2H), 5.09 (d, J = 12.4 Hz, 1H), 5.14 (d, J = 12.4 Hz, 1H), 6.44 (d, J = 1.6 Hz, 1H), 7.30-7.41 (m, 5H); ^13C NMR (100 MHz, CDCl_3): δ = 19.7, 22.4, 29.6, 43.8, 66.2, 95.4, 114.1, 128.1, 128.2, 128.5, 136.3, 176.1; HRMS (ESI) calcd. for C_{14}H_{15}ClNaO_2 [M+Na]^+: 273.0806; found: 273.0659.

Benzyl 2-(3-oxopropyl)cycloprop-2-ene-1-carboxylate (1ga):

R_f = 0.21 (Hexane/Et_2O = 90:10); Yield: 93% (Pale yellow oil)

^1H NMR (400 MHz, CDCl_3): 1.75 (t, J = 5.6 Hz, 1H), 1.79-1.86 (m, 2H), 2.21 (d, J = 1.2 Hz, 1H), 2.62 (t, J = 7.6 Hz, 2H), 3.66-3.70 (m, 2H), 5.09 (d, J = 12.4 Hz, 1H), 5.14 (d, J = 12.4 Hz, 1H), 6.38 (d, J = 1.6 Hz, 1H), 7.30-7.36 (m, 5H); ^13C NMR (100 MHz, CDCl_3): δ = 19.7, 21.6, 29.5, 61.7, 66.2, 94.7, 114.8, 128.1, 128.2, 128.5, 136.3, 176.6.

Benzyl 2-(3-oxopropyl)cycloprop-2-ene-1-carboxylate (1gb):

R_f = 0.63 (Hexane/Et_2O = 90:10); Yield: 95% (Pale yellow oil)

^1H NMR (400 MHz, CDCl_3): 2.22 (d, J = 1.6 Hz, 1H), 2.70-2.73 (m, 2H), 2.80-2.85 (m, 2H), 5.09 (d, J = 12.4 Hz, 1H), 5.14 (d, J = 12.4 Hz, 1H), 6.43 (d, J = 1.6 Hz, 1H), 7.31-7.36 (m, 5H), 9.75 (s, 1H); ^13C NMR (100 MHz, CDCl_3): δ = 17.9, 19.9, 40.7, 66.2, 95.6, 113.9, 128.1, 128.2, 128.5, 136.2, 175.9, 200.1.

Benzyl 2-(4-methylpent-3-en-1-yl)cycloprop-2-ene-1-carboxylate (1i):

R_f = 0.47 (Hexane/Et_2O = 95:5); Yield: 62% (Pale yellow oil)

^1H NMR (400 MHz, CDCl_3): 1.60 (s, 3H), 1.67 (s, 3H), 2.19 (d, J = 1.6 Hz, 1H), 2.23-2.28 (m, 2H), 2.49-2.54 (m, 2H), 5.08-5.16 (m, 3H), 6.35 (d, J = 1.6 Hz, 1H), 7.29-7.36 (m, 5H); ^13C NMR (100 MHz, CDCl_3): δ = 17.7, 19.8, 25.3, 25.7, 66.0, 94.2, 115.3, 122.8, 128.0, 128.1, 128.5, 132.9, 136.5, 176.4; HRMS (ESI) calcd. for C_{17}H_{31}O_2 [M+H]^+: 257.1481; found: 257.1536.
Characterization of compounds:

Benzy1-2-butyl-2-methylcyclopropane-1-carboxylate (2a\textsubscript{anti}):  
\[ R_f = 0.61 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 75% (Colorless oil)} \] 
\[ \text{^1H NMR (400 MHz, CDCl}_3\text{): 0.74-0.79 (m, 4H), 1.09 (s, 3H), 1.10-1.19 (m, 4H), 1.24-1.31 (m, 1H), 1.36-1.48 (m, 3H), 5.03 (s, 2H), 7.22-7.29 (m, 5H); ^13C NMR (100 MHz, CDCl}_3\text{): } \delta \text{ = 14.1, 22.2, 22.8, 24.1, 26.7, 27.6, 29.3, 31.9, 66.2, 128.1, 128.3, 128.5, 136.3, 172.7; HRMS (ESI) calcd. for C\textsubscript{16}H\textsubscript{25}O\textsubscript{2} [M+H]^+: 247.1698; found: 247.1701.} \] 
\[ \text{Note: The stereochemistry was determined through the NOESY experiment (spectrum available below).} \]

Benzy1-2-butyl-2-methylcyclopropane-1-carboxylate (2a\textsubscript{syn}):  
\[ R_f = 0.61 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 72% (Colorless oil)} \] 
\[ \text{^1H NMR (400 MHz, CDCl}_3\text{): 0.77-0.83 (m, 4H), 1.01 (t, J = 5.2 Hz, 1H), 1.1 (s, 3H), 1.18-1.29 (m, 6H), 1.47 (q, J = 2.4 Hz, 1H), 5.01 (d, J = 12.4 Hz, 1H), 5.07 (d, J = 12.4 Hz, 1H), 7.24-7.29 (m, 5H); ^13C NMR (100 MHz, CDCl}_3\text{): } \delta \text{ = 14.1, 16.2, 21.5, 22.7, 26.3, 27.2, 28.8, 40.5, 66.1, 128.0, 128.1, 128.5, 136.5, 172.7; HRMS (ESI) calcd. for C\textsubscript{16}H\textsubscript{25}O\textsubscript{2} [M+H]^+: 247.1698; found: 247.1700.} \] 
\[ \text{Note: The stereochemistry was determined comparing the NOESY and } ^{13}\text{C NMR experiments with the } 2a_{\text{anti}} \text{ (spectrum available below). In } 2a_{\text{syn}} \text{, due to the shielding effect of the ester group, carbon syn to it resulting in an upfield signal.} \]

Benzy1 3-butyl-3-methylpent-4-enoate (4a):  
\[ R_f = 0.59 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 72% (Colorless oil)} \] 
\[ \text{^1H NMR (400 MHz, CDCl}_3\text{): } \delta \text{ = 0.84 (t, J = 7.2 Hz, 3H), 1.09 (s, 3H), 1.16-1.23 (m, 4H), 1.34-1.38 (m, 2H), 2.34 (s, 2H), 4.91 (dd, J = 0.8, 18.0 Hz, 1H), 4.98 (dd, J = 0.8, 10.8 Hz, 1H), 5.06 (s, 2H), 5.78 (dd, J = 10.8, 18.0 Hz, 1H), 7.29-7.33 (m, 5H); ^13C NMR (100 MHz, CDCl}_3\text{): } \delta \text{ = 14.1, 23.2, 23.3, 26.3, 39.3, 40.5, 45.0, 65.9, 111.9, 128.1, 128.3, 128.5, 136.1, 145.7, 171.7; HRMS (ESI) calcd. for C\textsubscript{17}H\textsubscript{25}O\textsubscript{2} [M+H]^+: 261.1855; found: 261.1855.} \]

(S)-Benzy1 3-methyl-3-phenethylpent-4-enoate (S)-4b:  
\[ R_f = 0.47 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 70% (Colorless oil)} \] 
\[ \text{^1H NMR (400 MHz, CDCl}_3\text{): } \delta \text{ = 1.12 (s, 3H), 1.61-1.66 (m, 2H), 2.37 (s, 2H), 2.45 (dd, J = 6.4, 10.8 Hz, 2H), 4.93 (d, J = 17.6 Hz, 1H), 5.00 (d, J = 10.8 Hz, 1H), 5.02 (s, 2H), 5.80 (dd, J = 10.8, 17.6 Hz, 1H), 7.02-7.10 (m, 3H), 7.15-7.19 (m, 2H), 7.25-7.28 (m, 5H); ^13C NMR (100 MHz, CDCl}_3\text{): } \delta \text{ = 23.5, 30.7, 39.4, 42.6, 44.8, 66.1, 112.6, 125.6, 128.2, 128.3 (x2), 128.4, 128.5, 135.9, 142.6, 145.2, 171.5; HRMS (ESI) calcd. for C\textsubscript{23}H\textsubscript{24}O\textsubscript{2}Na [M+Na]^+: 331.1674; found: 331.1658; [α]D\textsubscript{25} (CHCl\textsubscript{3}, c = 0.22): 0.53°.} \] 
\[ \text{Note: The determination of the enantiomeric excess couldn’t be done on the } (S)-4b \text{ by HPLC with CHIRALPAK® AD-H, AY-H, IA or CHIRALCEL® OD columns, but after ozonolysis on the aldehyde } (S)-5b. \]
(S)-Benzy1 3-formyl-3-methyl-5-phenylpentanoate ((S)-5b):

$$R_t = 0.36 \text{ (Hexane/Et}_2\text{O} = 90:10); \text{ Yield: 62\% (Colorless oil)}$$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.14 \text{ (s, 3H), 1.68-1.82 (m, 2H), 2.38-2.50 (m, 2H), 2.52 (d, } J = 15.6 \text{ Hz, 1H), 2.63 (d, } J = 15.6 \text{ Hz, 1H), 5.03 (s, 2H), 7.00-7.01 \text{ (m, 2H), 7.08-7.11 (m, 1H), 7.15-7.19 (m, 2H), 7.22-7.29 \text{ (m, 5H), 9.49 (s, 1H); } ^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 19.4, 30.5, 37.7, 40.2, 47.9, 66.8, 126.3, 128.4, 128.6, 128.7, 128.8, 135.7, 141.5, 171.0, 204.1; \text{ HRMS (ESI) calcd. for } C_{26}H_{32}O_2 [M+H]^+ : 311.1647; \text{ found: 311.1650; e.r. = 96:4. The chiral sample was analyzed by HPLC using a CHIRALPAK } ^\text{®} \text{ AY-H column (10mmØx20mmL), n-hexane/isopropanol 90:10, 1 mL/min, 210nm. } t_R \text{ (major) = 9.78 min, } t_R \text{ (minor) = 8.12 min.}$

Ethyl 3-methyl-3-phenethylpent-4-enoate (4c):

$$R_t = 0.52 \text{ (Hexane/Et}_2\text{O} = 98:2); \text{ Yield: 71\% (Colorless oil)}$$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.13 \text{ (s, 3H), 1.17 (t, } J = 7.2 \text{ Hz, 3H), 1.63-1.68 \text{ (m, 2H), 2.31 (dd, } J = 13.6, 14.4 \text{ Hz, 2H), 2.46-2.50 \text{ (m, 2H), 4.04 (q, } J = 7.2 \text{ Hz, 2H), 4.94 (dd, } J = 0.8, 17.6 \text{ Hz, 1H), 5.02 (dd, } J = 1.2, 10.8 \text{ Hz, 1H), 5.80 (dd, } J = 10.8, 17.6 \text{ Hz, 1H), 7.08-7.10 \text{ (m, 3H), 7.18-7.21 \text{ (m, 2H); } ^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 14.3, 23.4, 30.7, 39.3, 42.6, 44.8, 60.9, 112.4, 125.6, 128.3 (x2), 142.7, 145.3, 171.6; \text{ HRMS (ESI) calcd. for } C_{16}H_{28}O_2 [M+H]^+ : 247.1698; \text{ found: 247.1634.}$

Benzyl 3-butyl-3-phenethylpent-4-enoate (4d):

$$R_t = 0.54 \text{ (Hexane/Et}_2\text{O} = 98:2); \text{ Yield: 64\% (Colorless oil)}$$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.84 \text{ (t, } J = 6.8 \text{ Hz, 3H), 1.17-1.28 (bs, 6H), 1.40-1.47 \text{ (m, 1H), 1.63-1.77 \text{ (m, 2H), 2.46-2.53 \text{ (m, 3H), 4.90 (d, } J = 17.6 \text{ Hz, 1H), 5.07-5.10 \text{ (m, 3H), 5.72 (dd, } J = 11.2, 17.6 \text{ Hz, 1H), 7.05-7.14 \text{ (m, 3H), 7.18-7.22 \text{ (m, 2H), 7.26-7.33 \text{ (m, 5H); } ^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 14.1, 23.2, 25.8, 30.3, 37.2, 39.5, 40.3, 42.3, 66.1, 113.2, 125.6, 128.2, 128.3, 128.4, 128.5, 128.6, 136.0, 142.8, 144.9, 171.6; \text{ HRMS (ESI) calcd. for } C_{24}H_{37}O_2 [M+H]^+ : 351.2280; \text{ found: 351.2319.}$

Ethyl 3-butyl-3-phenethylpent-4-enoate (4e):

$$R_t = 0.57 \text{ (Hexane/Et}_2\text{O} = 98:2); \text{ Yield: 68\% (Colorless oil)}$$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.84 \text{ (t, } J = 6.8 \text{ Hz, 3H), 1.16-1.20 (m, 7H), 1.34-1.45 \text{ (m, 2H), 1.57-1.75 \text{ (m, 2H), 2.36 (s, 2H), 2.41-2.56 \text{ (m, 2H), 4.05 (q, } J = 7.2 \text{ Hz, 2H), 4.88 (d, } J = 17.6 \text{ Hz, 1H), 5.05 (d, } J = 11.2, 17.6 \text{ Hz, 1H), 7.08-7.11 \text{ (m, 3H), 7.18-7.21 \text{ (m, 2H); } ^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 14.1, 14.3, 23.3, 25.8, 30.2, 37.1, 39.5, 40.4, 42.2, 60.0, 113.0, 125.6, 128.3, 128.3, 142.9, 145.0, 171.8; \text{ HRMS (ESI) calcd. for } C_{19}H_{26}O_2 [M+H]^+ : 289.2156; \text{ found: 289.2168.}$

Ethyl 3-methyl-3-benzylpent-4-enoate (4f):

$$R_t = 0.52 \text{ (Hexane/Et}_2\text{O} = 98:2); \text{ Yield: 75\% (Colorless oil)}$$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.04 \text{ (s, 3H), 1.17 (t, } J = 7.2 \text{ Hz, 3H), 2.19 (d, } J = 14 \text{ Hz, 1H), 2.27 (d, } J = 14 \text{ Hz, 1H), 2.65 (d, } J = 13.6 \text{ Hz, 1H), 2.70 (d, } J = 14.8 \text{ Hz, 1H), 4.04 (q, } J = 7.2 \text{ Hz, 2H), 4.82 (dd, } J = 0.8, 17.6 \text{ Hz, 1H), 4.94 (dd, } J = 1.2, 10.8 \text{ Hz, 1H), 5.83 (dd, } J = 10.8, 17.6 \text{ Hz, 1H), 7.07-7.09 \text{ (m, 2H), 7.13-7.20 \text{ (m, 3H); } ^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 14.3, 23.3, 40.0, 44.1, 46.8, 60.0, 112.3, 126.2, 127.7, 130.8, 137.8, 145.2, 171.8; \text{ HRMS (ESI) calcd. for } C_{15}H_{20}O_2 [M+H]^+ : 233.1542; \text{ found: 233.1519.}$
(S)-Benzyl 3-methyl-3-benzylpent-4-enoate ((S)-4g):

\[
\begin{align*}
\text{BnO}_2\text{C} & \quad \text{R}_1 = 0.49 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 72\% (Colorless oil)} \\
\text{1}^1\text{H NMR (400 MHz, CDCl}_3\text{): } & \delta = 1.04 \text{ (s, 3H), 2.25 (d, } J = 14.0 \text{ Hz, 1H), 2.32 (d, } J = 14.0 \text{ Hz, 1H), 2.65 (d, } J = 13.2 \text{ Hz, 1H), 2.69 (d, } J = 13.6 \text{ Hz, 1H), 4.80 (d, } J = 17.6 \text{ Hz, 1H), 4.92 (dd, } J = 1.2, 10.8 \text{ Hz, 1H), 5.02 (s, 2H), 5.82 (dd, } J = 10.8, 17.6 \text{ Hz, 1H), 7.03-7.05 (m, 2H), 7.12-7.18 (m, 3H), 7.24-7.28 (m, 5H); 1^3\text{C NMR (100 MHz, CDCl}_3\text{): } & \delta = 23.4, 40.1, 44.0, 46.8, 66.1, 112.5, 126.2, 127.7, 128.2, 128.4, 128.5, 130.8, 136.0, 137.7, 145.1, 171.6; HRMS (ESI) calcd. for C_{20}H_{23}O_2 [M+H]^+: 295.1657; found: 295.1693; [\alpha]_D^22: (CHCl_3, c = 0.14): 14.76\text{°.} \\
\text{Note: The determination of the enantiomeric excess couldn't be done on the (S)-4g by HPLC with CHIRALPAK AD-H, AYS-H, IA or CHIRALCEL OD columns, but after ozonolysis on the aldehyde (S)-5g.}
\end{align*}
\]

(S)-Benzyl 3-benzyl-3-methyl-4-oxobutanoate ((S)-5g):

\[
\text{BnO}_2\text{C} & \quad \text{R}_1 = 0.37 \text{ (Hexane/Et}_2\text{O = 90:10); Yield: 69\% (Colorless oil)} \\
\text{1}^1\text{H NMR (400 MHz, CDCl}_3\text{): } & \delta = 1.06 \text{ (s, 3H), 2.38 (d, } J = 15.6 \text{ Hz, 1H), 2.56 (d, } J = 16.4 \text{ Hz, 1H), 2.76 (d, } J = 13.6 \text{ Hz, 1H), 2.81 (d, } J = 13.6 \text{ Hz, 1H), 5.01 (d, } J = 12.4 \text{ Hz, 1H), 5.04 (d, } J = 12.4 \text{ Hz, 1H), 6.96-6.98 (m, 2H), 7.12-7.19 (m, 3H), 7.23-7.50 (m, 5H); 9.58 (s, 1H); 1^3\text{C NMR (100 MHz, CDCl}_3\text{): } & \delta = 19.7, 39.8, 41.7, 48.6, 66.8, 127.0, 128.5, 128.6, 128.7, 128.8, 130.6, 1357, 135.9, 171.1, 204.5; HRMS (ESI) calcd. for C_{19}H_{21}O_3 [M+H]^+: 297.1491; found: 297.1496; e.r. = 93.7. The chiral sample was analyzed by HPLC using a CHIRALPAK AD-H column (4.6mmØ×250mmL), n-hexane/isopropanol 90:10, 1 mL/min, 210 nm. t_R (major) = 7.85 min, t_R (minor) = 7.36 min.
\]

(S)-Benzyl 3-hexyl-3-benzylpent-4-enoate ((S)-4h):

\[
\begin{align*}
\text{BnO}_2\text{C} & \quad \text{R}_1 = 0.56 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 73\% (Colorless oil)} \\
\text{1}^1\text{H NMR (400 MHz, CDCl}_3\text{): } & \delta = 0.87 \text{ (t, } J = 7.2 \text{ Hz, 3H), 1.22-1.27 \text{ (m, 8H), 1.32-1.39 \text{ (m, 1H), 1.46-1.52 \text{ (m, 1H), 2.30 (d, } J = 14.8 \text{ Hz, 1H), 2.39 (d, } J = 14.8 \text{ Hz, 1H), 2.76 (d, } J = 13.2 \text{ Hz, 1H), 2.89 (d, } J = 13.2 \text{ Hz, 1H), 4.76 (d, } J = 18.0 \text{ Hz, 1H), 5.03 (d, } J = 11.2 \text{ Hz, 1H), 5.12 (s, 2H), 5.74 (dd, } J = 11.2, 18.0 \text{ Hz, 1H), 7.13-7.25 \text{ (m, 5H), 7.32-7.37 (m, 5H); 1^3\text{C NMR (100 MHz, CDCl}_3\text{): } & \delta = 14.1, 22.7, 23.9, 29.8, 31.8, 37.2, 39.1, 43.2, 43.6, 66.0, 113.0, 126.1, 127.7, 128.2, 128.4, 128.5, 130.9, 136.0, 137.8, 144.6, 171.9; HRMS (ESI) calcd. for C_{24}H_{23}O_2 [M+H]^+: 365.2427; found: 365.2475; [\alpha]_D^22: (CHCl_3, c = 0.24): 0.46°. \\
\text{Note: The determination of the enantiomeric excess couldn't be done on the (S)-4h by HPLC with CHIRALPAK AD-H, AYS-H, IA or CHIRALCEL OD columns, but after ozonolysis on the aldehyde (S)-5h.}
\end{align*}
\]

(S)-Benzyl 3-benzyl-3-hexyl-4-oxobutanoate ((S)-5h):

\[
\begin{align*}
\text{BnO}_2\text{C} & \quad \text{R}_1 = 0.41 \text{ (Hexane/Et}_2\text{O = 90:10); Yield: 72\% (Colorless oil)} \\
\text{1}^1\text{H NMR (400 MHz, CDCl}_3\text{): } & \delta = 0.85 \text{ (t, } J = 7.2 \text{ Hz, 3H), 1.20-1.24 \text{ (m, 8H), 1.57 (bs, 2H), 2.46 (d, } J = 16.4 \text{ Hz, 1H), 2.52 (d, } J = 16.4 \text{ Hz, 1H), 2.97 (s, 2H), 5.08 (d, } J = 12.0 \text{ Hz, 1H), 5.12 (d, } J = 12.0 \text{ Hz, 1H), 7.00-7.03 \text{ (m, 2H), 7.18-7.24 \text{ (m, 3H), 7.30-7.35 \text{ (m, 5H), 9.58 (s, 1H); 1^3\text{C NMR (100 MHz, CDCl}_3\text{): } & \delta = 14.2, 22.7, 23.9, 29.9, 31.7, 33.5, 36.3, 39.2, 52.4, 66.4, 126.9, 128.5, 128.6, 128.7, 128.8, 130.5, 135.9, 136.3, 171.4, 204.8; HRMS (ESI) calcd. for C_{24}H_{23}O_3 [M+H]^+: 367.2273; found: 367.2279; e.r. = 93.7. The chiral sample was analyzed by HPLC using a CHIRALCEL OD column (4.6mmØ×250mmL), n-hexane/isopropanol 99:1, 1 mL/min, 210 nm. t_R (major) = 9.62 min, t_R (minor) = 10.42 min.
\end{align*}
\]
(S)-Benzyl 3-hexyl-3-methylpent-4-enoate ((S)-4i):

\[
\begin{align*}
\text{Rf} &= 0.63 \text{ (Hexane/EtO = 98:2); Yield: 65\% (Colorless oil)} \\
^1\text{H NMR (400 MHz, CDCl}_3\text{): } &\delta = 0.85 \text{ (t, } J = 6.8 \text{ Hz, 3H), 1.09 \text{ (s, 3H), 1.19-1.25 (m, 8H), 1.33-1.37 (m, 2H), 2.34 (s, 2H), 4.90 (dd, } J = \text{ 0.8, 17.5 Hz, 1H), 4.96 (dd, } J = \text{ 1.2, 10.8 Hz, 1H), 5.06 \text{ (s, 2H), 5.78 (dd, } J = \text{ 10.8, 17.5 Hz, 1H), 7.28-7.33 \text{ (m, 5H); } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } &\delta = 14.3, 22.9, 23.5, 24.2, 30.1, 32.0, 39.5, 40.9, 45.2, 66.2, 112.1, 128.3, 128.5, 128.7, 136.3, 145.9, 171.9; HRMS (ESI) calcd. for C_{19}H_{29}O_2 [M+H]^+: 289.2156; \text{ found: } 289.2168; [\alpha]_D^0: \text{ (CHCl}_3, c = 0.32): 20.81^\circ. \\
\text{Note: The determination of the enantiomeric excess couldn't be done on the methylpentanoate.} \\
\end{align*}
\]

(R)-Benzyl 3-formyl-3-methylpent-4-enoate ((R)-4i):

\[
\begin{align*}
\text{Rf} &= 0.52 \text{ (Hexane/EtO = 90:10); Yield: 70\% (Colorless oil)} \\
\text{Spectral data of the title compound were identical to the (S)-Benzyl 3-formyl-3-methylpentanoate.} \\
\text{Note: The determination of the enantiomeric excess couldn't be done on the (R)-4i by HPLC with CHIRALPAK® AD-H, AY-H, IA or CHIRALCEL® OD columns, but after ozonolysis on the aldehyde (R)-5i.} \\
\end{align*}
\]

(R)-Benzyl 3-formyl-3-methylpentanoate ((R)-5i):

\[
\begin{align*}
\text{Rf} &= 0.52 \text{ (Hexane/EtO = 90:10); Yield: 72\% (Colorless oil)} \\
\text{Spectral data of the title compound were identical to the (S)-Benzyl 3-formyl-3-methylpentanoate. e.r. = 90:10. The chiral sample was analyzed by HPLC using a CHIRALCEL® OD column (4.6mm×250mmL), n-hexane/isopropanol 90:10, 1 mL/min, 210 nm. } t_R \text{ (major) = 5.43 min, } t_R \text{ (minor) = 5.19 min.} \\
\end{align*}
\]

Benzy1 6-((tert-butyldimethylsilyloxy)-3-methyl-3-vinylhexanoate (4j):

\[
\begin{align*}
\text{Rf} &= 0.62 \text{ (Hexane/EtO = 98:2); Yield: 70\% (Colorless oil)} \\
\text{Spectral data of the title compound were identical to the (S)-Benzyl 3-formyl-3-methylpentanoate. e.r. = 90:10. The chiral sample was analyzed by HPLC using a CHIRALCEL® OD column (4.6mm×250mmL), n-hexane/isopropanol 90:10, 1 mL/min, 210 nm. } t_R \text{ (major) = 5.24 min, } t_R \text{ (minor) = 5.91 min.} \\
\end{align*}
\]
Benzyl 6-chloro-3-methyl-3-vinylhexanoate (4k):

\[
\begin{align*}
\text{Rf} &= 0.46 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 71\% (Colorless oil)} \\
^{1}H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta &= 1.11 \text{ (s, 3H), 1.48-1.53 (m, 2H), 1.65-1.71 (m, 2H),} \\
& 2.36 \text{ (s, 2H), 3.43 (t, } J = 6.4 \text{ Hz, 2H), 4.94 (dd, } J = 0.8, 17.2 \text{ Hz, 1H), 5.02 (dd, } J = 0.8, 10.8 \text{ Hz, 1H),} \\
& 5.07 \text{ (s, 2H), 5.76 (dd, } J = 10.8, 17.2 \text{ Hz, 1H), 7.31-7.34 (m, 5H);} \\
^{13}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta &= 23.4, 27.6, 37.6, 38.9, 44.9, 45.4, 66.1, 112.7, 128.2, 128.4, 128.5, \\
& 135.9, 144.9, 171.3; \text{ HRMS (ESI) calcd. for C}_{16}H_{22}ClO_2 [M+H]^+: 281.1308; found: 281.1313}
\end{align*}
\]

Benzyl 3,7-dimethyl-3-vinylct-6-enoate (4l):

\[
\begin{align*}
\text{Rf} &= 0.49 \text{ (Hexane/Et}_2\text{O = 98:2); Yield: 64\% (Colorless oil)} \\
^{1}H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta &= 1.12 \text{ (s, 3H), 1.38-1.43 (m, 2H), 1.56 (s, 3H), 1.66} \\
& (s, 3H), 1.88-1.91 (m, 2H), 2.37 (s, 2H), 4.93 (dd, } J = 0.8, 17.6 \text{ Hz, 1H), 4.99-5.04} \\
& (m, 2H), 5.08 (s, 2H), 5.81 (dd, } J = 10.8, 17.6 \text{ Hz, 1H), 7.33-7.35 (m, 5H);} \\
^{13}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta &= 17.5, 22.8, 23.2, 25.6, 39.3, 40.6, 44.9, 66.0, 112.2, 124.4, 128.1, 128.3, 128.5, \\
& 131.4, 136.0, 145.4, 171.6; \text{ HRMS (ESI) calcd. for C}_{19}H_{27}O_2 [M+H]^+: 287.2019; found: 287.2006.}
\end{align*}
\]
$^1$H NMR spectrum of 1a (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1a (100 MHz, CDCl$_3$):
$^1{H}$ NMR spectrum of 1b (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1b (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched 1b:
$^1$H NMR spectrum of 1c (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1c (100 MHz, CDCl$_3$):
<sup>1</sup>H NMR spectrum of 1d (400 MHz, CDCl<sub>3</sub>):

<image>

<sup>13</sup>C NMR spectrum of 1d (100 MHz, CDCl<sub>3</sub>):

<image>
$^1$H NMR spectrum of 1e (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1e (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched 1e:

**Area Percent Report**

**Signal 1**: CDI C, Sig-210,4 Ref-360,20

<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
<th>[AU]</th>
<th>[AU] %</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 16.186 SB</td>
<td>0.4158</td>
<td>5249.35117</td>
<td>189.13080</td>
<td>56.7000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 16.850 SB</td>
<td>0.4550</td>
<td>5104.77556</td>
<td>166.59854</td>
<td>49.3000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Totals: 1.03549e4 305.72334

Results obtained with enhanced integrator:

*** End of Report ***

---

**Area Percent Report**

**Signal 1**: CDI C, Sig-210,4 Ref-360,20

<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
<th>[AU]</th>
<th>[AU] %</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 16.986 SB</td>
<td>0.3937</td>
<td>835.26436</td>
<td>33.56319</td>
<td>8.8041</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 16.512 SB</td>
<td>0.4813</td>
<td>1.17964e4</td>
<td>377.6343</td>
<td>95.1359</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Totals: 1.28598e4 411.15361

Results obtained with enhanced integrator:

*** End of Report ***
$^1$H NMR spectrum of 1f (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1f (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched 1f:
$^1$H NMR spectrum of 1g (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1g (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 1h (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1h (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 1ga (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1ga (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 1gb (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1gb (100 MHz, CDCl$_3$):
$^{1}$H NMR spectrum of 1i (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 1i (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 2$_a$anti (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 2$_a$anti (100 MHz, CDCl$_3$):
$^1$H-$^1$H NOESY spectrum of 2a<sub>anti</sub> (400 MHz, CDCl<sub>3</sub>):
HMQC spectrum of $\text{2a}_{\text{anti}}$: 
$^1$H NMR spectrum of 2a$_{syn}$ (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 2a$_{syn}$ (100 MHz, CDCl$_3$):
$^1$H-$^1$H NOESY spectrum of 2a$_{syn}$ (400 MHz, CDCl$_3$):
HMOC spectrum of 2a_{syn}:
$^1$H NMR spectrum of 4a (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4a (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4b (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4b (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 5b (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 5b (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched 5b:
$^1$H NMR spectrum of 4c (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4c (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4d (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4d (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4e (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4e (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4f (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4f (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4g (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4g (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 5g (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 5g (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched 5g:
$^1$H NMR spectrum of 4h (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4h (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 5h (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 5h (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched 5h:
$^1$H NMR spectrum of 4i (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4i (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 5i (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 5i (100 MHz, CDCl$_3$):
HPLC analysis of the racemic and enantioenriched S-5i:
HPLC analysis of the racemic and enantioenriched R-5i:
$^1$H NMR spectrum of 4j (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4j (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4k (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4k (100 MHz, CDCl$_3$):
$^1$H NMR spectrum of 4l (400 MHz, CDCl$_3$):

$^{13}$C NMR spectrum of 4l (100 MHz, CDCl$_3$):
$^1$H NMR spectrum for the reaction of 1d with PhLi for the formation of 4m:

$^{13}$C NMR spectrum for the reaction of 1d with PhLi for the formation of 4m:
$^1$H NMR spectrum for the reaction of 1j with C$_2$H$_3$MgBr for the formation of 4n:

$^{13}$C NMR spectrum for the reaction of 1j with C$_2$H$_3$MgBr for the formation of 4n: